This listing of claims will replace all prior versions and listings of claims in the application:

58. (Currently amended) A combination of substances in a liquid medium <u>for optimising and controlling the association of substances to extended surfaces</u>, comprising:

at least one first <u>surface-building</u> [[amphiphatic]] <u>amphipathic</u> substance selected from lipids, lipid-like materials and combinations thereof;

at least one second <u>surface-destabilising</u> [[amphiphatic]] <u>amphipathic</u> substance selected from [[edge-active]] <u>surface-active</u> substances, surfactants and combinations thereof; and

at least one third [[amphiphatic]] <u>amphipathic</u> substance selected from chain molecules <u>and macromolecules</u>;

wherein the first substance and the second substance form extended surfaces in contact with the medium,

wherein the solubility of the second [[amphiphatic]] <u>amphipathic</u> substance in the liquid medium is greater than the solubility of the first [[amphiphatic]] <u>amphipathic</u> substance in the liquid medium,

[[wherein the extended surfaces formed by the first substance are greater than the extended surfaces formed by the second substance,

wherein the extended surfaces formed by the first substance and the second substance combined are more extended than the extended surfaces formed by the first substance alone,]]

wherein molecules of the third substance associate with the extended surfaces formed by the first substance and the second substance,

wherein the presence of said at least one second substance in the combination increases the ability of the [[molecules of the third substance to associate with the extended surfaces formed by the at least one first substance and the at least one

SERIAL NO.: 09/555,986

Page 3 of 50

second substance]] extended surfaces formed by the at least one first substance and the at least one second substance to associate molecules of the third substance;

wherein the at least one first, at least one second and at least one third substance are different from each other.

- 59. (Previously presented) The combination of claim 58 wherein the extended surfaces are in the form of membrane surfaces.
- 60. (Previously presented) The combination of claim 58 wherein the extended surfaces formed by the first and second substance carry a net electric charge and wherein the third substance carries a net electric charge, the molecules of the third substance associating with the extended surfaces, and the net charge density of the surfaces and the net charge of the molecules associating with the surfaces having the same sign.
- (Previously presented) The combination of claim 58 wherein the extended 61. surfaces formed by the first and second substance are negatively charged and wherein the third substance is negatively charged.
- 62. (Previously presented) The combination of claim 58 wherein the extended surfaces formed by the first and second substance are positively charged and wherein the third substance is positively charged.
- 63. (Previously presented) The combination of claim 58 wherein the second substance causes increased flexibility of extended surfaces formed by an at least one first substance being capable of self-aggregating, when being mixed with said at least one first substance.

SERIAL NO.: 09/555,986

Page 4 of 50

- 64. (Previously presented) The combination of claim 58 wherein the first substance and the second substance differ in solubility on the average at least 10-fold.
- 65. (Previously presented) The combination of claim 58 wherein the first substance and the second substance differ in solubility on the average at least 100-fold.
- 66. (Previously presented) The combination of claim 58 wherein the second substance increases the curvature of an extended surface formed by the first substance being capable of self-aggregating when being incorporated into the extended surface, the concentration of the second substance being below 99% of the saturation concentration, or of that concentration above which the extended surface could not be formed, whichever is higher.
- 67. (Previously presented) The combination of claim 63 wherein the concentration of the second substance is at least 0.1 % of the relative concentration as defined in claim 66.
- 68. (Previously presented) The combination of claim 63 wherein the concentration of the second substance is from 1 to 80 percent of the relative concentration as defined in claim 66.
- 69. (Previously presented) The combination of claim 63 wherein the concentration of the second substance is from 10 to 60 percent of the relative concentration as defined in claim 66.
- 70. (Previously presented) The combination of claim 63 wherein the concentration of the second substance is from 20 to 50 percent of the relative concentration as defined in claim 66.

SERIAL NO.: 09/555,986

Page 5 of 50

- 71. (Previously presented) The combination of claim 66 wherein the surfaces have an average curvature, yielding an average radius between 15 nm and 5000 nm.
- 72. (Previously presented) The combination of claim 66 wherein the surfaces have an average curvature, yielding an average radius between 30 nm and 1000 nm.
- 73. (Previously presented) The combination of claim 66 wherein the surfaces have an average curvature, yielding an average radius between 40 nm and 300 nm.
- 74. (Previously presented) The combination of claim 66 wherein the surfaces have an average curvature, yielding an average radius between 50 nm and 150 nm.
- 75. (Previously presented) The combination of claim 66 wherein the surface is supported by a solid.
- 76. (Previously presented) The combination of claim 75 wherein the solid is a supporting surface of suitable curvature or size.
- 77. (Currently amended) The combination of claim 60 wherein the relative concentration of surface-related charged components is between 5 and 100 rel. mole% of the concentration of all surface-forming [[amphipats]] amphipaths taken together.
- 78. (Currently amended) The combination of claim 60 wherein the relative concentration of surface-related charged components is between 10 and 80 relative mole percent of the concentration of all surface-forming [[amphipats]] amphipaths taken together.
- 79. (Currently amended) The combination of claim 60 wherein the relative concentration of surface-related charged components is between 20 and 60 relative

SERIAL NO.: 09/555,986

Page 6 of 50

mole percent of the concentration of all surface-forming [[amphipats]] <u>amphipaths</u> taken together.

- 80. (Previously presented) The combination of claim 60 wherein the average charge density on the surface is between 0.05 Cb m<sup>-2</sup> and 0.5 Cb m<sup>-2</sup>.
- 81. (Previously presented) The combination of claim 60 wherein the average charge density on the surface is between 0.075 Cb m<sup>-2</sup> and 0.4 Cb m<sup>-2</sup>.
- 82. (Previously presented) The combination of claim 60 wherein the average charge density on the surface is between 0.1 Cb m<sup>-2</sup> and 0.35 Cb m<sup>-2</sup>.
- 83. (Previously presented) The combination of claim 60 wherein the concentration and the composition of electrolytes in which the first and the second substances are suspended, or from which the first and the second substances are adsorbed to a supporting surface, comprising mono or oligovalent ions, is chosen so as to maximise the positive effect of charge-charge interactions on the desired association and corresponds to ionic strength between I = 0.001 and I = 1.
- 84. (Previously presented) The combination of claim 60 wherein the concentration and the composition of electrolytes in which the first and the second substances are suspended, or from which the first and the second substances are adsorbed to a supporting surface, comprising mono or oligovalent ions, is chosen so as to maximise the positive effect of charge-charge interactions on the desired association and corresponds to ionic strength between I = 0.02 and I = 0.5.
- 85. (Previously presented) The combination of claim 60 wherein the concentration and the composition of electrolytes in which the first and the second substances are suspended, or from which the first and the second substances are adsorbed to a supporting surface, comprising mono or oligovalent ions, is chosen so as

SERIAL NO.: 09/555,986

Page 7 of 50

to maximise the positive effect of charge-charge interactions on the desired association and corresponds to ionic strength between I = 0.1 and I = 0.3.

- 86. (Currently amended) The combination according to claim 58 wherein the first substance is less soluble in the liquid medium, and/or being the surface-building and/or charge carrying [[amphipatic]] amphipathic substance in the system, is a lipid, whereas the second substance is more soluble in the liquid medium, and/or causing increased surface curvature, flexibility or adaptability and/or being the charge carrying substance, is a surfactant.
- 87. (Previously presented) The combination of claim 58 wherein the molecules are arranged in the form of minute fluid droplets suspended or dispersed in a liquid medium and surrounded by a coating of one or several layers of the first and second substances capable of self-aggregating and differing in solubility at least 10-fold in the liquid medium, such that the average diameter of homo-aggregates of the more soluble second substance or of hetero-aggregates of the first and second substances is smaller than the average diameter of homo-aggregates of the less soluble first substance.
- 88. (Currently amended) The combination of claim 58 wherein the total content of all [[amphipats]] amphipaths that form a surface is between 0.01 and 30 weight-% of the total dry mass of the aggregates.
- 89. (Currently amended) The combination of claim 58 wherein the total content of all [[amphipats]] amphipaths that form a surface is between 0.1 and 15 weight-% of the total dry mass of the aggregates.

SERIAL NO.: 09/555,986

Page 8 of 50

- 90. (Currently amended) The combination of claim 58 wherein the total content of all [[amphipats]] amphipaths that form a surface is between 1 and 10 weight-% of the total dry mass of the aggregates.
- 91. (Previously presented) The combination of claim 58 wherein the first substance is a biocompatible polar or non-polar surface-supporting lipid.
- 92. (Previously presented) The combination of claim 91 wherein the first extended surfaces forming substance is capable of forming bilayers.
- 93. (Previously presented) The combination of claim 58 wherein the first extended surfaces forming substance is selected from the group consisting of lipids, lipids from a biological source, corresponding synthetic lipids, and modifications of such lipids.
- 94. (Previously presented) The combination of claim 93 wherein the first extended surfaces forming substance is selected from the group consisting of glycerides, glycerophospholipids, isoprenoidlipids, sphingolipids, steroids, steroids, steroids, steroids, steroids, sulphur-containing lipids, a carbohydrate-containing lipids and half-protonated fluid fatty acids.
- 95. (Previously presented) The combination according to claim 93 wherein the first extended surfaces forming substance is selected from the group consisting of phosphatidylcholines, phosphatidylethanolamines, phosphatidylglycerols, phosphatidylinositols, phosphatidic acids, phosphatidylserines, sphingomyelins, sphingophospholipids, glycosphingolipids, cerebrosides, ceramidpolyhexosides, sulphatides, sphingoplasmalogenes, and gangliosides.

SERIAL NO.: 09/555,986

Page 9 of 50

- 96. (Previously presented) The combination according to claim 93 wherein the first extended surfaces forming substance is selected from the group consisting of diacyl-, dialkenoyl- and dialkyl-lipids.
- 97. (Previously presented) The combination according to claim 93 wherein the first extended surfaces-forming substance is selected from the group consisting of dioleoyl-lipids, dilinoleyl- lipids, dilinolenyl- lipids, dilinolenyl- lipids, diarachidoyl-lipids, dilauroyl- lipids, dimyristoyl- lipids, dipalmitoyl- lipids, distearoyl- lipids, and sphingosine- lipids.
- 98. (Previously presented) The combination of claim 58 wherein the second substance is a surfactant.
  - 99. Canceled.
- 100. (Previously presented) The combination of claim 98 wherein the surfactant is selected from the group consisting of nonionic, zwitterionic, anionic and cationic surfactants.
- 101. (Currently amended) The combination of claim 98 wherein the surfactant is selected from the group, consisting of long-chain fatty acids or long-chain fatty alcohols, alkyltrimethyl-ammonium salts, alkyldimethyl-ammonium salts, alkylmethyl-ammonium salts, alkylsulphate salts, monovalent salts of cholate, deoxycholates, glycocholates, glycodeoxycholates, taurodeoxycholates, taurocholates, acyl dimethyl-aminoxides, alkanoyl dimethyl-aminoxides, dodecyl dimethyl-aminoxide, alkyl-N-methylglucamides, alkanoyl-N-methylglucamides, N-alkyl-N,N-dimethylglycines, 3-(acyldimethylammonio)-alkanesulphonates, N-acyl-sulphobetaines, polyethylen-glycol-octylphenyl ethers, nonaethylen-glycol-octylphenyl ether, polyethylene-acyl ethers, nonaethylen-dodecyl ether, polyethyleneglycol-isoacyl ethers, octaethyleneglycol-isotridecyl ether, polyethylene-acyl ethers,

SERIAL NO.: 09/555,986

Page 10 of 50

octaethylenedodecyl ether, polyethyleneglycol-sorbitane-acyl esters, polyethylenglykol-20-monolaurate (Tween 20), polyethylenglykol-20-sorbitan-monooleate (Tween 80), polyhydroxyethylene-acyl ethers, polyhydroxyethylene-lauryl ethers, polyhydroxyethylene-myristoyl ethers, polyhydroxyethylene-cetylstearyl ethers, polyhydroxyethylene-oleoyl ethers, polyhydroxyethylen-4, or 6, or 8, or 10, or 12lauryl ethers (Brij series) [[, or in the corresponding esters, ]] polyhydroxyethylen-8stearate (Myrj 45), polyhydroxyethylen-laurates, polyhydroxyethylen-oleates, polyethoxylated castor oil 40 (Cremophor EL), sorbitane-monoalkylates, sorbitanemonolaurate, acyl-N-methylglucamides, alkanoyl-N-methylglucamides, decanoyl-Nmethylglucamide, dodecanoyl-N-methylglucamide, alkyl-sulphates, alkyl sulphate saltslauryl-sulphate, oleoyl-sulphate, sodium deoxycholate, sodium glycodeoxycholate, sodium oleate, sodium taurate, fatty acid salts, sodium elaidate, sodium linoleate, sodium laurate, lysophospholipids, n-octadecylene-glycerophosphatidic acid, octadecylene-phosphorylglycerol, octadecylene-phosphorylserine, n-acyl-glycerophosphatidic acids, lauryl glycero-phosphatidic acids, oleoyl-glycero-phosphatidic acid, n-acyl-phosphorylglycerol, lauryl-phosphorylglycerol, oleoyl-phosphorylglycerol, n-acyl-phosphorylserine, lauryl-phosphorylserine, oleolyl-phosphorylserine, ntetradecyl-glycero-phosphatidic acid, n-tetradecyl-phosphorylglycerol, n-tetradecylphosphorylserine, corresponding palmitoeloyl-, elaidoyl-, vaccenyl-lysophospholipids [[, corresponding short-chain phospholipids]], and surface-active polypeptides.

- 102. (Previously presented) The combination of claim 86 wherein the surface formed by the at least one first substance and the at least one second substance contains charged membrane components in the relative concentration range between 1 to 80 mole percent.
- 103. (Previously presented) The combination of claim 86 wherein the surface formed by the at least one first substance and the at least one second substance contains charged membrane components in the relative concentration range between 10 to 60 mole percent.

SERIAL NO.: 09/555,986

Page 11 of 50

104. (Previously presented) The combination of claim 86 wherein the surface formed by the at least one first substance and the at least one second substance contains charged membrane components in the relative concentration range between 30 to 50 mole percent.

- 105. (Currently amended) The combination of claim 58 wherein the surface-supporting at least one first substance is a phosphatidylcholine and/or a phosphatidylglycerol and the at least one second substance [[less capable of forming the extended surface]] is a lysophospholipid, a lysophosphatidic acid, methylphosphatidic acid, lysophosphatidylglycerol, lysophosphatidylcholine, a partially N-methylated lysophosphatidylethanolamine, a monovalent salt of cholate, deoxycholate, glycocholate, glycodeoxycholate, or a sufficiently polar sterol derivative, a laurate, myristate, palmitate, oleate, palmitoleate, elaidate or other fatty acid salt and/or a Tween-, a Myrj-, or a Brij-surfactant, or a Triton, a fatty acid sulphonate, sulphobetaine, -N-glucamide or -sorbitane surfactant.
- 106. (Previously presented) The combination of claim 87 wherein the average radius of the areas enclosed by said extended surfaces is between 15 nm and 5000 nm.
- 107. (Previously presented) The combination of claim 87 wherein the average radius of the areas enclosed by said extended surfaces is between 30 nm and 1000 nm.
- 108. (Previously presented) The combination of claim 87 wherein the average radius of the areas enclosed by said extended surfaces is between 40 nm and 300 nm.
- 109. (Previously presented) The combination of claim 87 wherein the average radius of the areas enclosed by said extended surfaces is between 50 nm and 150 nm.

SERIAL NO.: 09/555,986

Page 12 of 50

110. (Previously presented) The combination of claim 58 wherein the third substance associating with the extended surface comprises repeating subunits.

- 111. (Previously presented) The combination of claim 110 wherein the at least one third substance associating with the extended surface is a chain molecules, selected form the group consisting of oligomers or polymers.
- 112. (Previously presented The combination of claim 111 wherein the chain molecules have an average molecular weight above 800 Daltons.
- 113. (Previously presented The combination of claim 111 wherein the chain molecules have an average molecular weight above 1000 Daltons.
- 114. (Previously presented) The combination of claim 111 wherein the chain molecules have an average molecular weight above 1500 Daltons.
- 115. (Previously presented) The combination of claim 110 wherein the third substance is of biological origin.
- 116. (Previously presented) The combination of claim 110 wherein the third substance is bioactive.
- 117. (Previously presented) The combination of claim 58 wherein the third substance associates with the membrane-like extended surface by inserting itself in the interface and/or interfaces between the membrane and the liquid medium in contact with said membrane.
- 118. (Previously presented) The combination of claim 111 wherein the content of the chain molecules is between 0.001 and 50 relative percent compared to the mass

of adsorbent surface, whereby the specific ratio value decreases with increasing molar mass of the chain molecules.

- 119. (Previously presented) The combination of claim 111 wherein the content of the chain molecules is between 0.1 and 35 relative percent compared to the mass of adsorbent surface, whereby the specific ratio value decreases with increasing molar mass of said chain molecules.
- 120. (Previously presented) The combination of claim 111 wherein the content of said chain molecules is between 0.5 and 25 relative percent compared to the mass of adsorbent surface, whereby the specific ratio value decreases with increasing molar mass of said chain molecules.
- 121. (Previously presented) The combination of claim 111 wherein the content of the chain molecules is between 1 and 20 relative percent compared to the mass of adsorbent surface, whereby the specific ratio value decreases with increasing molar mass of the chain molecules.
- 122. (Previously presented) The combination of claim 111 wherein the chain molecules are proteins, and at least a part of said molecules is associated with the surface, provided that such part has at least three segments or functional groups with a propensity to bind to said surface.
- 123. (Previously presented) The combination of claim 111 wherein the chain molecules are polynucleotides.
- 124. (Previously presented) The combination of claim 123 wherein the polynuleotides are selected from the group consisting of DNA and RNA, in the natural form or after chemical, biochemical, or genetic modification.

SERIAL NO.: 09/555,986

Page 14 of 50

125. (Previously presented) The combination of claim 111 wherein the chain molecules are polysaccharides with at least partial propensity to interact with the surface either in the natural form or after chemical, biochemical, or genetic modification.

126. (Currently amended) The combination of claim 58 wherein the third substance acts as an adrenocorticoid, a ß-[[adrenolyte]]adrenolytic drug, an androgen an antiandrogen, an antiparasite, an anabolic, an anaesthetic, an analgesic, an analeptic, an antiallergenic, an antiarrhythmic, an antisclerotylosis, an antiasthmatic, a bronchospasmolytic, an antibiotic, an antidrepressant, an antipsychotic, an antidiabetic, an antidote, an antiemetic, an antiepileptic, an antifibrinolytic, an anticonvulsive, an anticholinergic, an enzyme, a coenzyme or corresponding inhibitor, an antihistamine, an antihypertensive agents, a biological inhibitor of drug activity, an antihypotensive, an anticoagulant, an antimycotic, an antimyasthenic, an agent against Parkinson or Alzheimer, an antiphlogistic, an antipyretic, an antirheumatic, an antiseptic, a respiratory analeptic or a respiratory stimulant, a anti-bronchitis agent, a cardiotonic, a chemotherapeutic agent, a coronary dilator, a cytostatic, a diuretic, a ganglion-blocker, a glucocorticoid, an anti-influenza agent, a haemostatic, a hypnotic, an immunoglobulin or its fragment, an immunologically active substance, a bioactive carbohydrate, a bioactive carbohydrate derivative, a contraceptive, an antimigraine agent, a mineralocorticoid, a morphine-antagonist, a muscle relaxant, a narcotic, a neurotherapeutic, a neuroleptic, a neurotransmitter or its antagonist, a peptide, a peptide derivative, an ophthalmic agents, a sympathomimetic agent or a sympatholytic agent, a para- sympathomimetic agent or a para- sympatholytic agent, a protein, a proteine derivative, a psoriasis drug, a neurodermatitis drug, a mydriatic, a psychostimulant, [[rhinologicum]] naso-active drug, a sleep-inducing agent or its antagonist, a sedating agent, a spasmolytic, tuberculostatic, urologic agent, a vasoconstrictor or vasodilator agents, a antiviral, a wound-healing substance, or a combination thereof.

SERIAL NO.: 09/555,986

Page 15 of 50

127. (Previously presented) The combination of claim 58 wherein the third

substance is a growth modulating substance.

128. (Previously presented) The combination of claim 58 wherein the third

substance has immunomodulating properties, and is selected from the group

consisting of antibodies, cytokines, lymphokines, chemokines and correspondingly

active parts of plants, bacteria, viruses, pathogens, immunogens, or parts or

modifications thereof.

129. (Previously presented) The combination of claim 58 wherein the third

substance is a bio-catalyst.

130. (Previously presented) The combination of claim 58 wherein the third

substance is an enzyme, or a co-enzyme.

131. (Previously presented) The combination of claim 58 wherein the third

substance is a recognition molecule, selected from the group consisting of adherins,

antibodies, catenins, selectins, chaperones, or parts thereof.

132. (Previously presented) The combination of claim 58 wherein the third

substance is a hormone.

133. (Previously presented) The combination of claim 58 wherein the third

substance is insulin.

134. (Previously presented) The combination of claim 133 wherein the insulin

is human recombinant or humanised insulin.

SERIAL NO.: 09/555,986

Page 16 of 50

- 135. (Previously presented) The combination of claim 133 wherein the content of insulin is between 1 and 500 I.U. insulin/mL.
- 136. (Previously presented) The combination of claim 133 wherein the content of insulin is between 20 and 400 I.U. insulin/mL.
- 137. (Previously presented) The combination of claim 133 wherein the content of insulin is between 50 and 250 I.U. insulin/mL.
- 138. (Previously presented) The combination of claim 58 wherein the third substance is interleukin suitable for the use in humans or animals.
- 139. (Previously presented) The combination of claim 138 wherein the third substance is selected from the group comprising IL-2, IL-4, IL-8, IL-10, and IL-12.
- 140. (Previously presented) The combination of claim 138 wherein the combination contains between 0.01 mg and 20 mg interleukin/mL.
- 141. (Previously presented) The combination of claim 138 wherein the combination contains between 0.1 mg and 15 mg interleukin/mL.
- 142. (Previously presented) The combination of claim 138 wherein the combination contains between 1 mg and 10 mg interleukin/mL.
- 143. (Previously presented) The combination of claim 183 wherein the interferon is selected from the group comprising Interferon alpha, beta and gamma.
- 144. (Previously presented) The combination of claim 183 wherein the composition contains up to 20 relative wt-% interferon.

SERIAL NO.: 09/555,986

Page 17 of 50

145. (Previously presented) The combination of claim 58 wherein the third substance is nerve growth factor (NGF).

- 146. (Previously presented) The combination of claim 145 wherein the NFG is human recombinant NGF.
- 147. (Previously presented) The combination of claim 145 wherein the combination contains up to 25 mg NGF/mL suspension.
- 148. (Previously presented) The combination of claim 145 wherein the combination contains up to 25 relative weight percent NGF.
- 149. (Previously presented) The combination of claim 145 wherein the combination contains between 0.1 and 15 relative weight percent NGF.
- 150. (Previously presented) The combination of claim 145 wherein the combination contains between 1 and 10 relative weight percent NGF.
- 151. (Previously presented) The combination of claim 58 wherein the third substance is immunoglobulin (Ig).
- 152. (Previously presented) The combination of claim 151 wherein the Immunoglobulin (Ig) is used in the form of an intact antibody, part of it, or a biologically acceptable and active modification thereof.
- 153. (Previously presented) The combination of claim 151 wherein the combination contains up to 25 mg immunoglobulin(Ig)/mL suspension.
- 154. (Previously presented) The combination of claim 151 wherein the combination contains up to 25 relative weight percent Ig relative to total lipid.

SERIAL NO.: 09/555,986

Page 18 of 50

- 155. (Previously presented) The combination of claim 151 wherein the combination contains between 0.1 and 15 relative weight percent Ig.
- 156. (Previously presented) The combination of claim 151 wherein the combination contains between 1 and 10 relative w-% Ig.
- 157. (Previously presented) A method of preparing a combination according to claim 58 in the form of a formulation of a biologically, cosmetically and/or pharmaceutically active agent, comprising:

selecting the at least one first and the at least one second substance, forming extended surfaces, when the first and second substances are combined in contact with said medium,

selecting the at least one third substance,

allowing the molecules of the third substance to associate with the extended surfaces formed by the at least one first and the at least one second substance.

- 158. (Previously presented) The method of claim 173 or 174 wherein the means of controlled mechanical fragmentation are selected from the group comprising filtration, pressure change or mechanical homogenisation, shaking, stirring, and mixing.
- 159. (Previously presented) The method of claim 157 wherein the combination of surface forming at least one first and at least one second substances is permitted to adsorb to suitable supporting solid surfaces, and then with the liquid medium by adding one substance after another or several at a time, whereby at least one of the later surface-forming steps is carried out in the presence of the agent that subsequently associates with the solid-supported surface.

SERIAL NO.: 09/555,986

Page 19 of 50

160. (Previously presented) The method of claim 159 wherein the adsorbing surfaces or their precursors, whether suspended in a liquid medium or supported by a solid, are first prepared by steps which include sequential mixing of the surface forming molecules of the at least one first and at least one second substances, and the associating molecules of the at least one third substance are then added and permitted to associate with the said surfaces.

- 161. (Previously presented) A method for the preparation of a formulation for non-invasive application of active agents, wherein surfaces capable of associating with the active agent are formed from at least one first substance being an amphiphilic substance, at least one hydrophilic fluid, at least one second substance being an edge active substance or surfactant, and at least one third substance being said active agent, wherein the method comprises separately mixing the at least one first substance, the at least one second substance, the at least one hydrophilic fluid and the at least one third substance, followed by combining the resulting mixtures to subsequently induce the formation of the surfaces which associate with the active agent.
- 162. (Currently amended) The method of claim 161 wherein the active agent is selected from the group consisting of anti-diabetic agents, growth factors, immunomodulators, enzymes, recognition molecules, adrenocorticoid, and [[adrenolyte]] adrenolytic drugs.
- 163. (Previously presented) The method of claim 161 wherein the amphiphilic substances are either used as such, or dissolved in a physiologically compatible polar fluid, comprising water or water-miscible fluids, or in a solvation-mediating agent, together with a polar solution.
- 164. (Previously presented) The method of claim 163 wherein the polar solution contains at least one edge-active substance or a surfactant.

SERIAL NO.: 09/555,986

Page 20 of 50

165. (Previously presented) The method of claim 163 wherein the formation of

said surfaces is induced by substance addition into a fluid phase, evaporation from a

reverse phase, by injection or dialysis, with the aid of mechanical stress,.

166. (Previously presented) The method of claim 163 wherein the formation of

said surfaces is induced by filtration, the filtering material having pores sizes between

 $0.01 \, \mu m$  and  $0.8 \, \mu m$ .

167. (Previously presented) The method of claim 163 wherein the formation of

said surfaces is induced by filtration, the filtering material having pores sizes between

 $0.02 \, \mu m$  and  $0.3 \, \mu m$ .

168. (Previously presented) The method of claim 163 wherein the formation of

said surfaces is induced by filtration, the filtering material having pores sizes between

 $0.05 \, \mu m$  and  $0.15 \, \mu m$ .

169. (Previously presented) The method of claim 158 wherein several filters

are used sequentially or in parallel.

170. (Previously presented) The method of claim 163 herein said agents and

carriers are made to associate, at least partly, after formation of the adsorbing surface.

171. The method of claim 163 wherein said surfaces, with which the agent

molecules associate, are prepared just before the application of the formulation, if

convenient from a suitable concentrate or a lyophylisate.

172. (Currently amended) A method for providing a pharmaceutical

composition comprising:

in a combination of claim 58, providing the extended surfaces in the form of

membranes formed by the at least one first substance and the at least one second

SERIAL NO.: 09/555,986

Page 21 of 50

substance surrounding miniature droplets, wherein the at least one third substance being a drug associates with <u>the exterior surface of</u> said droplet surface to be carried by said droplets to the place where the drug is intended to act.

- 173. (Previously presented) The method of claim 157 further comprising: utilizing controlled mechanical fragmentation to form extended surfaces.
- 174. (Previously presented) The method of claim 157 further comprising the step of generating the extended surfaces by means of controlled mechanical fragmentation in the presence of the third substance or before the addition of the third substance, such that the third substance associates with the extended surfaces formed by controlled mechanical fragmentation.
- 175. (Previously presented) The combination of claim 65 wherein the concentration of the second substance is at least 0.1 % of the relative concentration as defined in claim 66.
- 176. (Previously presented) The combination of claim 65 wherein the concentration of the second substance is from 1 to 80 percent of the relative concentration as defined in claim 66.
- 177. (Previously presented) The combination of claim 65 wherein the concentration of the second substance is from 10 to 60 percent of the relative concentration as defined in claim 66.
- 178. (Previously presented) The combination of claim 65 wherein the concentration of the second substance is from 20 to 50 percent of the relative concentration as defined in claim 66.

SERIAL NO.: 09/555,986

Page 22 of 50

179. (Previously presented) The combination of claim 66 wherein the concentration of the second substance is at least 0.1 % of the relative concentration as defined in claim 66.

- 180. (Previously presented) The combination of claim 66 wherein the concentration of the second substance is from 1 to 80 percent of the relative concentration as defined in claim 66.
- 181. (Previously presented) The combination of claim 66 wherein the concentration of the second substance is from 10 to 60 percent of the relative concentration as defined in claim 66.
- 182. (Previously presented) The combination of claim 66 wherein the concentration of the second substance is from 20 to 50 percent of the relative concentration as defined in claim 66.
- 183. (Currently amended) The combination of claim [[1]] 58, wherein said at least one third substance is interferon being suitable for use in humans or animals.
- 184. (Previously presented) The combination of claim 183, wherein interferon is included in an amount ranging from about 0.1 to about 15 mg interferon/mL.
- 185. (Previously presented) The combination of claim 183, wherein interferon is included in an amount ranging from about 1 to about 10 mg interferon/mL.
- 186. (Currently amended) The use of the combination of claim 58 for medicinal or biological applications, wherein said combination is applied to the human or animal body, or brought into such body, by appropriate conventional means, either directly or using conventional excipients.

SERIAL NO.: 09/555,986

Page 23 of 50

- 187. (Currently amended) The use of the combination of claim 58 for the preparation of drug carriers or drug depots by providing said extended surfaces in the form of membranes surrounding miniature droplets, wherein the at least one third substance associating with said droplet surface is a drug, and applying said droplets to the place where the drug is intended to act.
- 188. (Currently amended) The use of the combination of claim 58 for bioengineering or for genetic manipulations, wherein said combination is introduced into the system by conventional means, such that it initially preserves the adsorption of chain molecules on said complex extended surfaces.
- 189. (Currently amended) The use of the combination of claim 58 for separation technology, (bio)processing or diagnostic purposes, wherein a conventional separation, bioprocessing or diagnostic material is covered or replaced by said complex adaptable surface with conventional means, such as spontaneous aggregate adsorption or covalent coupling.
- 190. (Currently emended) The use of the combination of claim [[58]] <u>87</u> to stabilize surface-associating molecules and/or in catalysing processes which involve molecules in the surface-associated state <u>by providing the extended surfaces in the form of membranes formed by the at least one first substance and the at least one second substance surrounding miniature droplets, wherein the at least one third substance is the associating active molecule associated with said droplet surface.</u>
- 191. (Currently amended) The use of the combination of claim 190 for chain molecules [[that are at least partially amphipathic]].
- 192. (Previously presented) The use of the combination of claim 191, wherein the chain molecules are proteins, polypeptides, polynucleotides or polysaccharides.

SERIAL NO.: 09/555,986

Page 24 of 50

- 193. (Currently amended) The use of the combination of claim 58 to affect the kinetics and/or the reversibility of association or dissociation between surfaceassociating molecules and a complex, adaptable surface, wherein said surface is an essential part of an application system.
- 194. (New) The use according to claim 186 wherein said conventional means are selected from the group of oral dosage forms, suppositories, simple or depot injections, pulmonaries, nasal or dermal applications.
- 195. (New) The use according to claim 188 said conventional means are selected from the group of addition of the combination into the broth and pre-coating of growth supporting surfaces.
- 196. (New) The use according to claim 189, wherein said conventional means are selected from spontaneous aggregate adsorption and covalent coupling.
- 197. (New) The use according to claim 193, wherein said application system is selected from the group of conventional kits, dosage forms and preparations.
- 198. (New) The use according to claim 193, wherein the kinetics and/or the reversibility of association or dissociation between surface-associating molecules and a complex, adaptable surface is affected by surface coating or addition.